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Why flies? Inexpensive public engagement exercises to explain the value of basic biomedical research on *Drosophila melanogaster*

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Pulver SR, Cognigni P, Denholm B, Fabre C, Gu WX, Linneweber G, Prieto-Godino L, Urbančič V, Zwart M, Miguel-Aliaga I. Why flies? Inexpensive public engagement exercises to explain the value of basic biomedical research on *Drosophila melanogaster*. *Adv Physiol Educ* 35: 384–392, 2011; doi:10.1152/advan.00045.2011.—Invertebrate model organisms are powerful systems for uncovering conserved principles of animal biology. Despite widespread use in scientific communities, invertebrate research is often severely undervalued by laypeople. Here, we present a set of simple, inexpensive public outreach exercises aimed at explaining to the public why basic research on one particular invertebrate, the insect *Drosophila melanogaster*, is valuable. First, we designed seven teaching modules that highlight cutting-edge research in *Drosophila* genetics, metabolism, physiology, and behavior. We then implemented these exercises in a public outreach event that included both children and adults. Quantitative evaluation of participant feedback suggests that these exercises 1) teach principles of animal biology, 2) help laypeople better understand why researchers study fruit flies, and 3) are effective over a wide range of age groups. Overall, this work provides a blueprint for how to use *Drosophila* as a vehicle for increasing public awareness and appreciation of basic research on genetically tractable insects in particular and invertebrates in general.

fruit flies; genetics; neuroscience; metabolism; physiology; animal behavior

CONSERVED PRINCIPLES IN BIOLOGY have often been uncovered by studying invertebrates. In the fields of genetics (Refs. 22 and 26; for a review, see Ref. 3), physiology (Refs. 10, 27, 40, and 41; for a review, see Ref. 12), and animal behavior (Refs. 7 and 9; for a review, see Ref. 23) in particular, invertebrate biologists have a long track record of making discoveries that are translatable to a wide range of animal phyla. Studying invertebrates has helped researchers understand core operating principles, not just in other invertebrates, but also in “higher” vertebrates (including humans). Furthermore, invertebrate research is clearly not “past its prime.” On the contrary, invertebrate researchers continue in the present day to make important contributions to the scientific record. Often, these discoveries rapidly become the basis for research in other types of animals and even biomedical research on humans (3, 28a).

Despite a long and continually growing list of achievements by scientists studying invertebrate animals, members of the general public are often unaware of the utility of these organisms as model systems in biology. Laypeople often simply fail to see the usefulness of studying an animal that looks different

from them. They appear to be especially skeptical of the idea that basic research on invertebrates can actually help inform and channel biomedical research that benefits humans. In one extreme case, a politician actually highlighted basic research on fruit flies as an example of wasteful government spending that has “little or nothing to do with the public good” (28).

There is a clear need for invertebrate biologists to engage with the public and explain at a grassroots level why their research is of value. One approach to doing this is to put forward selected model organisms as animal “ambassadors” to the public. This would give nonscientists opportunities to see the actual animals involved and scientists a chance to showcase cutting-edge experiments. Due to its genetic and experimental tractability, the fruit fly *Drosophila melanogaster* is one of the most important model organisms for studying genetics, physiology, and animal behavior. *Drosophila* is particularly well suited as an ambassador model of this type because 1) simple and rapid experiments can be performed to demonstrate important biological concepts, 2) they pose no threat to human health, and 3) they are easy and inexpensive to obtain, rear, and transport.

The goal of the present work was to show how to use *Drosophila* as a tool to demonstrate the usefulness of basic biomedical research to laypeople. We designed a suite of simple teaching modules that highlight state of the art research in *Drosophila* genetics, physiology, and animal behavior and then implemented these exercises in a public outreach event. Here, we report feedback from a wide range of age groups on the effectiveness of these exercises. Overall, this work is important because it helps bridge a communication gap between research scientists and the general public.

TEACHING MODULES

We designed seven teaching modules that highlight *Drosophila* biology and modern research techniques. Each module can stand alone or be combined with others as needed depending on equipment availability and the audience. Each exercise was designed to make a small focused set of “take-home points,” be suitable for both adults and children, and last no more than 5–10 min. Below we present how to implement each module and conclude with general information on how to rear fruit flies and make genetic crosses.

Module 1: How a Fruit Fly Is Made and What It Looks Like

This exercise allowed the visitors to become familiar with the life cycle of a fruit fly and the morphology of wild-type and mutant flies. Visitors were shown a cartoon with embryonic, larval, pupal, and adult stages. They then had the chance to see each of these stages under a dissection microscope (Fig. 1A).

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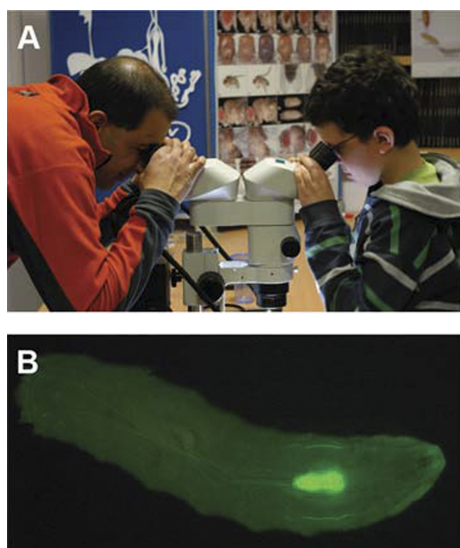


Fig. 1. A: adults and children were able to observe fly eggs, larvae, and adult flies using a two-headed dissection microscope. The poster behind them allowed them to identify specific mutations. B: a third-instar larva expressing membrane-tagged green fluorescent protein in the central nervous system (genotype *nSyb-Gal4/UAS-CD8GFP*). Note the green nerves projecting to peripheral muscles in addition to the bright green signal in the ventral nerve cord.

Visitors were shown wild-type animals as well as mutant strains carrying gene mutations that affected eye pigment or size/shape (*white* and *Drop* mutations, respectively), wing morphology (*Curly* and *Serrate* mutations), and bristle shape (*Stubble* mutation). Visitors were asked to identify seven differences between flies: the genitalia and sex combs of male versus female flies and the five mutations described above. Visitors were told that the latter were the result of a mutation in a single gene. Overall, this module aimed to 1) illustrate the concept that genetic mutations can give rise to visible alterations in external morphology and 2) show that their short generation time (~10 days) allows multiple crosses that can be followed over several generations to be performed so that the genes responsible for specific alterations can be mapped in a relatively short period of time. The module also served as an introduction to the more general concept that flies have genes that are homologous to those found in humans.

Materials and methods. The following fly stocks were used in *module 1*: *Oregon-R-C* (wild-type flies, Bloomington no. 5), *w¹¹¹⁸*; *Dr/TM6B*, *Sb*, *P{Dfd-GMR-nvYFP}*, and *w¹¹¹⁸*; *Kr/CyO*; *D/TM3*, *Ser* (mutant flies, Bloomington nos. 23232 and 7198, respectively). A two-headed Olympus SZX7 dissecting microscope was used to observe basic anatomic features (Fig. 1A). Fly embryos from these stable stocks were collected after placing 10–20 fruit flies in laying pots: plastic containers covered with an apple juice agar plate (a Sterilin, 50-mm single vent, no. 122 petri dish with a set apple juice-agar solution as detailed below) topped with some yeast paste (recipe below). Larvae and pupae were collected from aged embryo collections (96 h after egg laying and 120 h after egg laying) and were presented in similar petri dishes containing the apple juice-agar medium. Adult flies were put in small media-free petri dishes and were observed as freely behaving animals.

APPLE JUICE PLATES. For 507 ml of solution (~50 plates), mix and boil 11.5 g dextrose (158968, Sigma), 11.5 g agar

(LP0013, Oxoid), 7 ml nipagin (H3647, Sigma, used as a stock solution of 100 g/l in ethanol), 125 ml apple juice, and 375 ml deionized water. Remove scum by skimming the surface and pour the solution into small petri dishes.

YEAST PASTE. Baker's yeast and deionized water were mixed in a 1:2 ratio according to weight.

Module 2: Visualizing a Fruit Fly's Internal Organs Using Green Fluorescent Protein

The purpose of this exercise was to make visitors appreciate that even the small and apparently simple fly larva has complex internal organs: brain, muscles, gut, heart, and the functional equivalents of kidneys. It also showed that these organs can be visualized by genetically targeting expression of a green fluorescent protein (GFP) (8) to specific tissues. Visitors were able to see a variety of larvae on a computer screen, which collected a live signal from a camera attached to a fluorescent dissecting microscope. Larvae with single labeled organs were obtained by expressing GFP under the control of tissue-specific *Gal4* drivers (Fig. 1B; see *Materials and methods*). Once visitors had become familiar with the anatomy of specific internal organs, they were prompted to identify labeled organs in other larvae. We explained that by combining this approach to visualize internal organs with genetic manipulation, we can identify genes required for the formation of specific organs. These genes may be conserved in humans, and thus the fly may help shed light on the mutations underlying human developmental disorders. The example used to illustrate this particular point was a mutant lacking the *robo* gene, in which the anatomy of the nervous system [visualized in green with *fasciclin2-GFP* (31)] is severely disrupted. This larva displays anatomic defects similar to that resulting from mutation of a related gene (ROBO3) in humans, which is characterized by impaired hindbrain development and results in paralysis of lateral eye movement and horizontal gaze palsy with progressive scoliosis (18).

Materials and methods. The following fly stocks were used as stable fly stocks in *module 2*: *hand-GFP* [pericardial cells (37)] and *fasciclin2-GFP* (31). Males from the following crosses were crossed to virgin females containing a *UAS-CD8-GFP* transgene (Bloomington no. 5130) to visualize specific cells/organs in their F1 larval progeny: *G203-Gal4* [muscles (11)], *Cha-Gal4* [central nervous system (CNS) (34)], *byn-Gal4* [hindgut (39)], and *CtB-Gal4* [Malpighian tubules (38)]. *robo* mutant embryos were used to visualize axon defasciculation and were obtained by crossing males containing the *robo¹* mutation (36) and the *fasciclin2-GFP* reporter (31) to *robo²* virgin females (36) (final genotype of F1 progeny: *fasciclin2-GFP; robo¹/robo²*). Embryos or larvae were collected as described in *module 1*. In this case, the agar plates contained no apple juice to improve image quality. Larvae were visualized using a Leica MZ16F fluorescence dissecting microscope attached to a DFC420C color camera. A computer connected to this camera allowed the live visualization of larvae using Leica Application Suite software.

Module 3: Flies Exhibit Complex Behaviors, Which Are Under Neuronal Control

This module showed that 1) *Drosophila* display complex behaviors and 2) these are controlled by specific cells in the fly

brain. Courtship behavior (14) was used to illustrate these concepts, primarily because it encompasses a sequence of stereotypical actions [e.g., smell, taste, and execution of a courtship song through wing vibration (Supplemental Material, Supplemental Movie S1)] that are required for mating success and are controlled by a group of neurons expressing the *fruitless* gene (33).¹

After a short introduction based on a cartoon illustrating the different courtship steps, visitors observed the differential anatomy of single male and female flies under a dissecting microscope and were prompted to observe the behaviors of single males paired with single females in a small chamber. Courtship behaviors were observed live under a dissecting microscope either by eye or with an attached digital camera (see *Materials and methods* for details). Participants were encouraged to identify specific actions performed by the males and how the female fly responded to them (for example, when females are receptive to a courtship display, they slow down their movements). Visitors also listened to a recorded male song on the computer. Finally, they were told that by unraveling how different *fruitless*-expressing neurons work together to coordinate a stereotyped behavioral sequence in males and females, we may begin to understand the principles of how animal nervous systems (including our own) are organized and can be used to generate complex behaviors.

Together, these three modules provided a descriptive overview of the fly's anatomy and its experimental advantages. They also began to introduce basic concepts such as the link between genetic manipulation and its effect on external morphology, internal organs, and behavior. The following four modules provide more advanced, often hands-on, examples of how to use specific genetic, physiological, and metabolic methods to investigate the functions of fly organs and what they can teach us about how our own body works.

Materials and methods. Before the activity, wild-type male and female flies were separated at eclosion and kept in separate tubes. Three-day-old wild-type (Canton-S, Bloomington stock no. 1) flies were used, and two fly pairs per group were planned in case one pair failed to court. A Leica S6E dissection microscope attached to a Stingray F-033B camera (Allied Vision Technologies) was used. The camera was connected to a laptop with software (Quicktime Pro or AstroIICD). Two courtship chambers were used, although the experiment could also be conducted in regular fly tubes. A pooter was used to move single flies from the tubes to the courtship chamber without a need for anesthesia.

The male song (Supplemental Audio File S1) was previously recorded using a clip-on metal microphone (frequency response: 20 Hz to 16 kHz, impedance: 2 k Ω) by attaching it to one of the two openings of a plastic tube, adding a male and a female fly through the other opening, and closing the opening with cotton wool.

Module 4: Manipulating Neuronal Activity in *Drosophila* Larvae Using Channelrhodopsin-2

This activity illustrates the level of precision with which we can study the function of specific cells in the fruit fly brain.

This was achieved by remotely activating selected sets of neurons using optogenetic techniques (for a review, see Ref. 24) and examining the effects on larval crawling. For this purpose, the blue light-gated ion channel channelrhodopsin-2 (ChR2) (25, 35) was expressed in two different sets of neurons using the *Gal4-UAS* system (5). We used two different *Gal4* driver lines to express ChR2: *elav-Gal4* resulted in pan-neuronal expression of the *UAS-ChR2* transgene, whereas *pick-pocket (ppk)-Gal4* led to ChR2 expression in a subset of “nociceptive” neurons that sense noxious stimuli and mediate escape responses (17). Participants first observed how these two different genotypes (as well as wild-type animals) crawled over an agar surface in the absence of blue light. Illumination with a pulse of blue light (~488 nm) led to the activation of neurons expressing ChR2. Pan-neuronal activation of ChR2 caused tetanic paralysis and shortened larval body length due to contraction of all body muscles. In contrast, activation of ChR2 in nociceptive cells lead to lateral rolling (17) and/or an increase in crawling speed that brought the animal quickly out of the illuminated field (escape response). Behavioral responses to light pulses in wild-type animals were minimal and consisted primarily of a short pause in crawling at the onset of the light pulse. Nociceptive neuron stimulation was placed in an ecological context by showing a short video of a larva escaping from a parasitic wasp by performing a lateral roll (17). Hence, visitors were able to see that we can elicit specific behaviors observed in the wild by turning on specific sets of neurons. We also explained that when synaptic transmission is blocked in these cells, larvae are not capable of performing escape behaviors in response to wasp attacks (17). This makes the point that nociceptive neurons are necessary and sufficient for an adaptive escape behavior.

It is important to note that *Drosophila* larvae have visual systems and can perceive blue light. During these exercises, we emphasized the importance of conducting control experiments, in this case measuring behavioral responses to blue light in wild-type animals. By looking at wild-type responses to light pulses, participants were able to clearly see that endogenous responses to light pulses were minimal compared with those evoked by ChR2 stimulation.

Materials and methods. ChR2-expressing flies were placed in food-containing vials 5 days in advance of experiments and raised at 25°C. *UAS-H134R-ChR2* (30) virgin females were collected and crossed to *ppk-Gal4* (Bloomington no. 32078) (17) males in laying pots. Flies with ChR2 expression in all neurons (*w;elav-Gal4, UAS-H134R-ChR2*, Bloomington no. 8765 for *elav-Gal4*) were placed directly into laying pots. Agar plates were changed daily the week leading up to the experiment, and the plates were kept so that the F1 progeny (second or early third instar larvae) were available on the demonstration day. For all ChR2 experiments, we supplemented fly food with 1 mM all-*trans*-retinal (a cofactor necessary for proper folding of ChR2, Toronto Research Chemicals, North York, CA). The preparation of retinal-containing fly food is described in detail in Ref. 16. Guidelines for rearing flies and making genetic crosses are found below and in Refs. 16 and 19.

Larvae were visualized using a MZ16F fluorescence dissecting microscope, DFC420C color camera, and Leica Application Suite software (Leica). Blue light pulses were given by manual control of shutter timing. Previous work has demonstrated the feasibility of doing similar experiments with an

¹ Supplemental Material for this article is available at the *Advances in Physiology Education* website.

inexpensive LED based system (29). Participants were also shown a video of a *Drosophila* larva performing escape behaviors to elude parasitization by a wasp. This movie was part of a previous research publication (17).

Module 5: Manipulating Neuronal Activity in Adult *Drosophila* Using a Temperature-Sensitive Ion Channel

Like the previous module, this activity shows that we can use genetics to install “switches” in fruit fly neurons that allow researchers to remotely control neural activity in freely behaving animals. In this case, we made use of flies expressing the transient receptor potential channel (dTRPA1) in specific neuronal populations. dTRPA1 is a temperature-sensitive cation channel that opens in response to moderate warming (e.g., 23–29°C). This allows researchers to remotely control brain activity in poikilotherms (i.e., “cold-blooded animals”) simply by changing the ambient temperature (15, 30).

We made use of two kinds of flies: wild-type control flies and flies expressing dTRPA1 in neurons containing the excitatory neurotransmitter ACh (Cha-GAL4) (34). Participants were given a brief introduction to the use of dTRPA1 as a tool to remotely control neural activity in flies. We then asked them to make a hypothesis about what would happen behaviorally if a large number of excitatory cells in the fly brain were activated at once with dTRPA1. Participants themselves then placed the vials of experimental and control lines (unlabeled) in the water bath and observed the resulting behaviors by eye. After ~1 min, dTRPA1 flies fell to the floor of the vial and showed uncoordinated spasms of leg and wing movement for ~60 s, followed by paralysis. When removed from the hot water bath, dTRPA1 flies recovered and showed normal locomotor activity after 2–3 min.

This module illustrated how unregulated activity in an animal’s nervous system is not adaptive and leads to seizures in flies just the same as it does in humans. A large part of an animal’s nervous system is dedicated to preventing this from happening. When neural activity is not regulated properly, this leads to pathologies. We explained to visitors that understanding seizure-like behaviors in less complex model organism such as the fruit fly could help us better understand how and why they happen in humans.

Materials and methods. Two weeks before the exercise, we crossed virgin female *UAS-dTRPA1* (Bloomington no. 26263) (15) flies to male *Cha-GAL4* flies (Bloomington no. 6798) (34). F1 progeny have the heat-sensitive ion channel dTRPA1 expressed primarily in cholinergic neurons. Cholinergic neurons are widespread in the *Drosophila* CNS, and fast cholinergic synapses are the primary excitatory synapse in the fly CNS (6). F1 progeny were then grown on standard cornmeal-based fly food through embryonic, larval, pupal, and adult stages at 22–23°C. Before the exercise (0.5–1 h), we transferred adult F1 progeny and a wild-type control line (Oregon-R-C, Bloomington no. 5) to vials without food and labeled with numbers alone. Before the exercise, we calibrated a hot plate to maintain tap water in a plastic container at 29–31°C. Foodless vials containing experimental and control lines were kept at room temperature (23–23°C) until participants visited the station. During each module, vials containing dTRPA1 and control flies were submerged in the warmed tap water, and the resulting behaviors were observed.

Module 6: the *Drosophila* Excretory System

Excretory systems regulate the composition of body fluids in multicellular animals. Most people are unaware that flies have an excretory system that is functionally equivalent to the human kidney. The main goals of this exercise were to show 1) what a real live fly excretory system looks like, 2) demonstrate that the fly excretory system is a similar but simplified version of more complex organs (like our own kidney), and 3) demonstrate how we (as scientists) use the fly version of a kidney (i.e., the Malpighian tubules and nephrocytes) to understand how organs are built and how they function.

Observations of the fly excretory system were demonstrated for two developmental stages. The larval excretory system was revealed by making use of a genetic line with a mutation causing Malpighian tubules to appear bright red (Fig. 2A). Fly larvae were used because their transparent cuticle permits clear visibility of all internal organs. To show the embryonic excretory system and to demonstrate how fly Malpighian tubules develop, we showed a movie of embryonic development where tubules had been marked with GFP (Supplemental Movie S2). The movie spanned ~5 h of development (compressed to ~10 s) and illustrated the changes in organ shape that accompany the maturation of the renal system during embryogenesis. A living fly embryo was presented to illustrate the scale at which we were filming.

Structural and functional comparisons between the fly excretory system and the vertebrate kidney were highlighted. A number of visual props were used to illustrate the structure and function of vertebrate kidneys. These included a pig

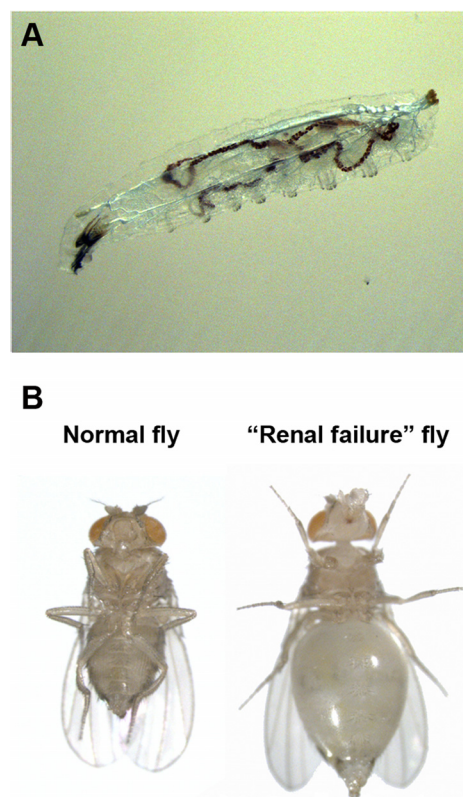


Fig. 2. A: a third-instar red mutant larva. Note the red renal tubules. B: when the renal tubules fail to develop appropriately, adult flies experience renal failure and retain excessive amounts of fluid.

kidney (purchased from the local butcher) cut in half to reveal the inner structure of the organ as well as visual displays to highlight the important function of the human kidney in 1) osmoregulation (8 liters of water were displayed, the approximate amount of water filtered through our kidneys every hour), 2) salt balance (1.3 kg of salt was displayed, the amount of salt that is filtered through our kidneys every day), and 3) toxin clearance [a large petri dish containing “toxic” material (green washing liquid) representing toxins removed from circulation].

To demonstrate that the *Drosophila* excretory system functions in a similar way to human kidneys, we presented examples of living adult flies with normally functioning Malpighian tubules alongside flies with a genetic mutation that disrupts Malpighian tubule function (Fig. 2B) (unpublished observations). In these mutants, fluid balance is disrupted, and, as a consequence, the flies dramatically balloon due to excessive fluid retention. We explained that this outcome is similar to the excessive bodily swelling observed in human patients with kidney failure. It was explained that by studying the effects of genetic manipulation in a simple organ system, we begin to understand fundamental principles of how more complex organs are generated and function.

Materials and methods. A mutant stock with red Malpighian tubules (*red¹*, Bloomington stock no. 565) (13) was used for all experiments. Larvae were reared and collected as described in previous modules. They were presented in a small petri dish with agar and viewed using a two-headed SZX7 dissection microscope using $\times 20$ – 80 magnification.

Module 7: *Drosophila* as a Model for the Study of Nutrition, Digestive Function, and Metabolism

This module explored the similarities between the digestive tracts of fruit flies and humans. Participants were first shown a schematic of the two tracts, which highlighted anatomic and functional similarities. The advantages of using the fruit fly as model organism to study digestion and metabolism were described. We stressed that working with flies gives us the ability to test multiple conditions or manipulate specific genes and organs and the relative simplicity of a smaller system makes it easy to uncover core conserved principles. The small size of the *Drosophila* gut was reinforced by showing a real dissected fly gut on a microscope slide (a few millimeters long) and then comparing it with the size of an uncoiled human gut (~ 5 m, or the length of the room in which the event was held). By looking at the fly gut under the microscope, visitors could identify the major portions of the digestive tract (crop, small intestine, and large intestine).

The function of the digestive tract was demonstrated by showing two metabolic assay plates prepared in advance (see *Materials and methods*) and asking the visitors what they thought the small colored dots on the plastic were. When, after occasional chuckling, visitors correctly identified them as feces, they were invited to observe the difference between the two plates and speculate about their origin. The two plates differed in the color of excreta, reflective of a change in acidity (10). The different acidity was revealed by the pH indicator dye used (see *Materials and methods* for details) and resulted from feeding the flies different diets: diets that they were then invited to taste for themselves in liquid form. This illustrated

how a simple experiment using this model system can uncover the effect of different diets on internal metabolism.

Finally, each visitor was invited to take home a freshly prepared metabolic assay plate containing a single male fly and one of the two fly food diets (which are indistinguishable by eye). After a few days, the color of fecal deposits would allow them to identify the recipe of the food contained in the plate. It should be noted that these diets are nontoxic to humans. Consequently, there are no safety concerns or hazards associated with this activity.

Materials and methods. EQUIPMENT AND GUT DISSECTION. We used a S6E dissection microscope (Leica) for all dissections. Wild-type males (as described above) were fed on fly food containing 0.5% bromophenol blue sodium salt (B5525, Sigma) for 2 days before the event. Shortly before the event, the digestive tracts were dissected in saline, taking care not to pierce them, and mounted in glycerol.

SINGLE FLY METABOLIC ASSAY PLATES. Two different recipes were prepared with the following ingredients. “Food 1” contained 36 g/l sucrose (S9378, Sigma), 54 g/l autolysed yeast flakes (T. P. Drewitt), 5 g/l bromophenol blue sodium salt (B5525, Sigma), 15 ml/l nipagin (H3647, Sigma, used as a stock solution of 100 g/l in ethanol), and 10 g/l agar (LP0013, Oxoid). “Food 2” contained 90 g/l sucrose, 5 g/l bromophenol blue sodium salt, 15 ml/l nipagin, and 10 g/l agar. Flies fed *food 1* produce blue (more basic) deposits, whereas flies fed *food 2* excrete yellow/green (acidic) deposits.

Each recipe was prepared in distilled water, brought to a pH of 5.5, boiled, and dispensed into petri dishes (35×10 -mm dish, 153066, Nunc). Once set, each portion of food was cut with a razor blade into six wedges, and a single wedge was placed into a new petri dish. A single anesthetized wild-type male was added to each petri dish, which was then sealed with two drops of silicone (RS 692-542, RS Components) between the plate and the lid (Fig. 3). Two such plates (containing the two different recipes) were prepared 2 days in advance to show the results of the metabolic assay to the public. The remaining plates were prepared just before the event, so that there would be no initial fecal deposits.

EDIBLE “FLY FOOD.” Versions of the two different recipes used for the metabolic assay were prepared in plastic cups using food-grade ingredients from a local supermarket. *Food 1* contained refined sugar, active baker’s yeast, and blue food coloring (indigo carmine) in mineral water. *Food 2* contained refined sugar and blue food coloring in mineral water.

General Fly Rearing and Genetic Crosses

Wild-type and mutant stocks (for details of the genotypes used, see the specific modules) were raised in clear plastic 3×1 -in. vials (purchased from T. P. Drewitt, London, UK) containing 8 ml of a standard cornmeal-agar diet (1.2% autolysed yeast, 5.5% cornmeal, 6% dextrose, and 0.55% agar supplemented with 0.18% nipagin and 2.9 ml/l propionic acid) unless otherwise indicated and were kept in 25°C incubators (although it would also be possible to rear flies at room temperature). To obtain flies of a desired genotype, genetic crosses between males and virgin females were conducted as described in http://flystocks.bio.indiana.edu/Fly_Work/culturing.htm. The F1 progeny of these crosses consisted of embryos or larvae. For details of how to stage larvae to obtain first,

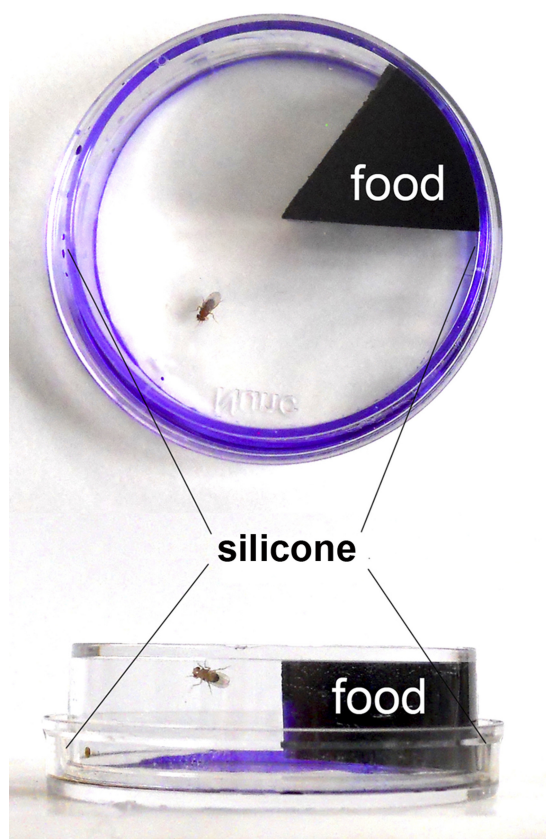


Fig. 3. Experimental setup for the metabolic assay. See Module 7: *Drosophila* as a Model for the Study of Nutrition, Digestive Function, and Metabolism (Materials and methods) for details.

second, or third larval instars, see http://en.wikipedia.org/wiki/Drosophila_melanogaster.

IMPLEMENTATION AND EVALUATION

We implemented these exercises in a public outreach event within the framework of the Cambridge Science Festival 2011 (<http://comms.group.cam.ac.uk/sciencefestival/>). The event was attended by 53 people, representing all age groups (Fig. 4A). Participants were received in groups of up to 12 people every hour to optimize access to stations. Each group first listened to a 5-min talk introducing *Drosophila* as a model organism in biomedical research. The talk stressed that *Drosophila* has been a premier model system in biological research for over 100 yr, primarily because it is relatively easy to manipulate the fruit fly genome and interpret the results of genetic experiments. After this talk, people were free to spend 5–10 min at each of the seven stations. At each station, a demonstrator explained the purpose of each module and, where appropriate, conducted/helped participants perform experiments.

After their visit, participants were asked to fill in a questionnaire designed to evaluate the technical and conceptual aspects of the exercise, and 46 participants (86%) did so. Both children (0–18 yr old, $n = 22$) and adults (19 yr and over, $n = 24$) participated (Fig. 4A). The exercises worked in a technical sense (Fig. 4C) and were interpretable and fun for children and adults (Fig. 4, B–E). The modules also facilitated the understanding of basic biology research in general (Fig. 4, F and G) and fruit fly research in particular (Fig. 4H).

Assessment of Modules

Modules 1–3 provided a descriptive overview of the fruit fly's anatomy and its experimental advantages. They also introduced basic concepts such as the link between genetic manipulation and its effect on external morphology, internal organs, and behavior. These exercises provide essential baseline information, but they were not as compelling for laypeople as the more advanced modules ($P = 0.0005$ by a two-tailed binomial test; Fig. 4B). Strikingly, no participants singled out module 1 (basic morphology and genetic markers) as their favorite. This module consisted of learning about the fruit fly life cycle, looking at basic morphology, and examining mutant flies with altered morphologies. This kind of activity forms the bases of most introductory genetic classroom exercises (11) and is traditionally the way most university students are first exposed to *Drosophila* as a model organism. But our results suggest that such descriptive approaches are less compelling than those based on function—both for adults and children.

In modules 4 and 5, we introduced the idea that genetics can be used to install ways of remotely controlling the activity of specific neural circuits in behaving animals. Previous work (1, 29) has shown the effectiveness of these techniques in undergraduate teaching laboratories. As in previous work, both light and heat activation (using ChR2 and dTRPA1, respectively) of large neuronal populations evoked robust, easy to observe behavioral phenotypes. Our response data suggest that children especially appeared to appreciate dTRPA1 experiments (module 5; Fig. 4B). This may be due to the facts that 1) dTRPA1-induced behavioral phenotypes are readily visible to the naked eye and/or 2) children were encouraged to take an active role in performing experiments in this module.

Module 6 was focused on showing the similarities between the fruit fly renal system and the vertebrate kidney. This exercise emphasized the points that 1) all metazoan animals have to regulate the composition of their internal fluids and 2) the organs that animals use to do this can show remarkable morphological and functional conservation across animal phyla. We also stressed that our understanding of the basic principles of renal system formation and function are incomplete. The movie of Malpighian tubule development (Supplemental Movie S2) and the examples of mutant flies with defects in Malpighian tubule function (Fig. 2) were presented as components of ongoing research. This proved to be useful in a number of ways. First, it provided an opportunity to convey the excitement of undertaking cutting-edge research. Second, it provided a hook for the more curious participants to ask specific questions about our research (e.g., “Does kidney development start from one cell or multiple cells?”, “Does the fly renal system have stem cells?”, “How well does the fly ‘kidney’ work if it is the wrong shape?”). Finally, it allowed us to explain that basic science in simple models like the fly are necessary to improve our understanding before cures or treatments for human kidney diseases can be made.

Module 7 introduced the idea that we can use *Drosophila* as a model organism to study how food is metabolized. The activities were interactive and well received by all age groups (Fig. 4B). Small children were especially interested in trying fly food for themselves and obtaining a “fly pet.” The most common questions centered on how long the flies in the metabolic assay would live and how to maintain them in a

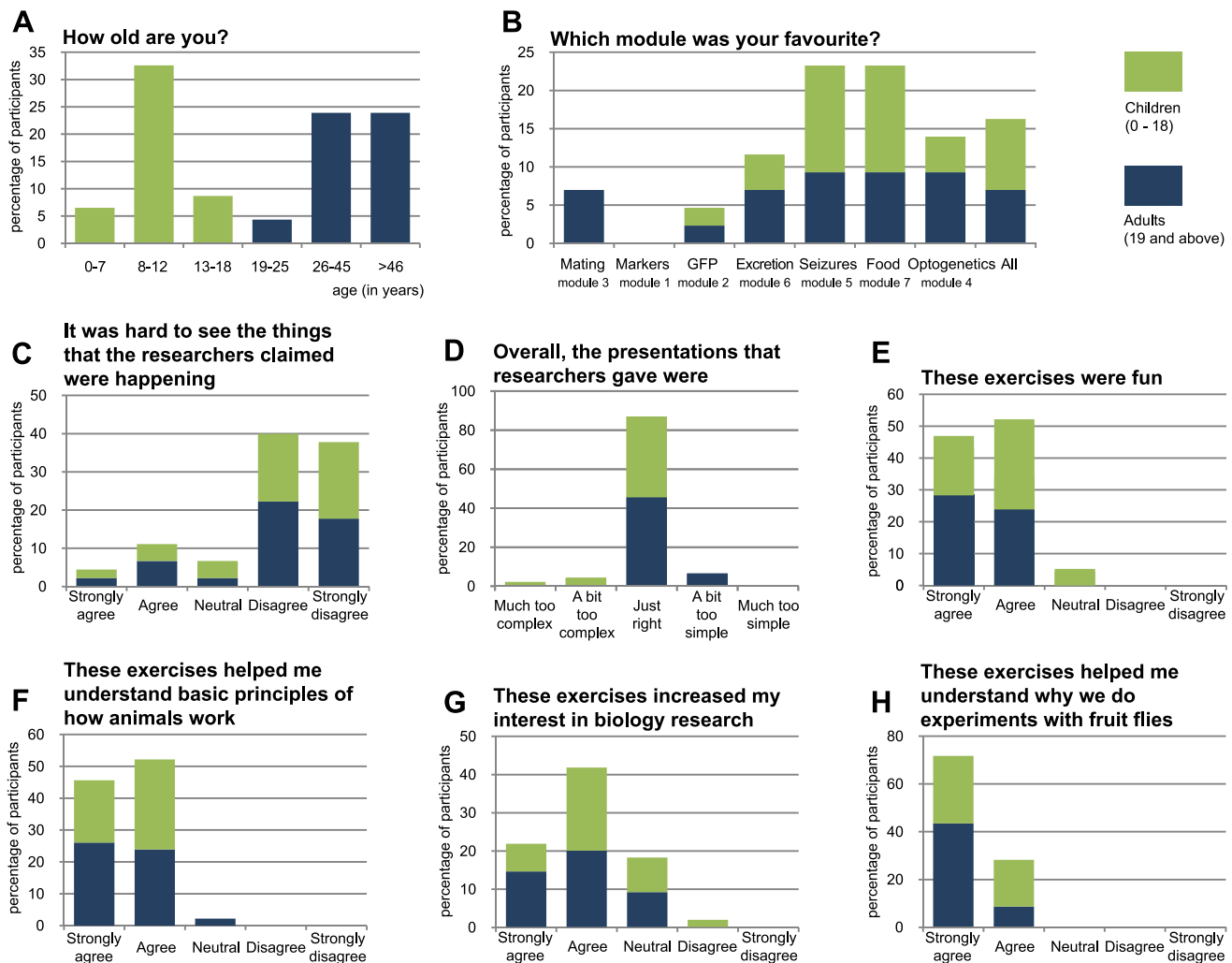


Fig. 4. Quantitative evaluation of participant feedback. *A*: demographic breakdown of participants. *B*: module preference, presented as a write-in question. *C*–*H*: responses to a set of six questions about the effectiveness and enjoyment of the event, evaluated on a Likert scale. All values are represented as percentages of the total responses.

healthy condition. We also received many inquiries about the normal lifespan of flies and their dietary habits. Without prompting, several participants asked whether certain human metabolic disorders also apply to flies (e.g., “Can flies be diabetic?”) and whether it was possible to study these diseases in flies. In the light of this, a good addition to this activity would be to use transgenic flies with manipulations of the insulin pathway (4) [and/or insulin-producing cell ablation (32)] that show metabolic abnormalities as examples of fly models for human metabolic diseases.

Challenges and Advantages of Working With Adults and Children at the Same Time

Most teaching exercises are tailored for specific age groups. This is appropriate for the structure of modern elementary and secondary schools; however, targeting one age group by definition reduces the number of people who can benefit. We set out to create exercises that would teach principles of biology and help laypeople of all ages understand why basic research on an invertebrate is valuable. We implemented all modules in a situation where we were talking to both small children and

adults at the same time. Each exercise was designed to be detailed enough to hold the attention of adults while also being fun and interactive enough to hold the attention of children. Our response data suggest that we accomplished these goals. First, a large majority of participants (both children and adults) were able to clearly see the biological phenomena being presented by researchers (Fig. 4C). Second, an overwhelming number of both children and adults found the level of complexity in our presentations to be optimal (Fig. 4D). Third, all adults and all but one child either agreed or strongly agreed that the exercises were fun (Fig. 4E). Fourth, over 95% of participants either agreed or strongly agreed that the exercises helped them understand fundamental principles of biology (Fig. 4F). Fifth, 100% of participants felt that the modules helped them understand why researchers study *Drosophila* (Fig. 4H). Finally, a smaller (but still substantial) majority of participants reported that these modules also increased their interest in biological research in general (Fig. 4G).

Our success at communicating with multiple age groups could be attributed to several specific factors. First, presenters made conscious efforts to spend equal amounts of time speak-

ing to young children and adults during each module. If one age group or individual started to monopolize the discussion, the presenter would step in and make an attempt to engage with others in the group. Second, the number of people participating in any one module was small (~12 people), and presenters did not have to communicate with all age levels all at once. Within each module, there were usually only two to three different age levels, so presenters could adapt their presentation style to make sure that no participants were left behind. Third, presenters had to give the same presentation multiple times to new people. This gave presenters chances to experiment with different ways of communicating with young and old and see first hand what worked and what did not. Finally, presenters made an effort to engage with participants of all ages as equal partners in scientific discovery. We made an effort to treat participants of all ages as collaborators as opposed to pupils.

Working with multiple age groups posed a major challenge for presenters, but it also had unexpected benefits. Specifically, it appeared to hone and focus the communication skills of the presenters. After the exercise, all 10 presenters (all co-authors on this report) agreed that talking to both children and adults was extremely helpful for streamlining presentations at each module. The presence of children pushed researchers to simplify their message, but the presence of adults ensured that important messages were still conveyed.

Maximizing Flexibility and Minimizing Cost

One advantage of the exercises presented here is that they can be run together as a complete unit or each stand alone. Presenters can pick and choose from an array of modules (that cover several topics in biology) depending on the availability of resources, expertise of presenters, and interests of the participants. It is important to note that we used research-grade microscopy equipment in several of our teaching modules. We felt this was justified given that the equipment used is common in research laboratories and that one of the points of these exercises was to suggest ways for researchers to mobilize available resources for public outreach. That said, we were also careful to design some exercises (notably *modules 5–7*) that require very little in the way of specialized equipment. Importantly, our response data do not suggest that the use of research-grade equipment increases the popularity of a module. If anything, our data suggest the opposite (Fig. 4B).

Responsible Anthropomorphizing

One danger of these exercises is that it is very easy for presenters to begin overanthropomorphizing. A degree of anthropomorphizing can be a useful teaching tool, and, obviously, one of the points of these exercises is to draw parallels between fruit fly and human biology. But in some cases, if presenters are careless, it can lead to serious misconceptions. For example, one presenter drew parallels between dTRPA1-induced spasms in flies and seizures in humans with epilepsy. While the overall behavioral phenotypes are similar, it is not appropriate to declare dTRPA1-expressing flies as “epileptic flies,” which is what some participants immediately did. In another example, the term “fly kidneys” was used as a device to highlight the parallel between the renal systems of flies and vertebrates. However, the kidney is an organ specific to vertebrates. It was stressed during the presentations that flies have

Malpighian tubules, an organ that is distinct from but performs similar functions to the vertebrate kidney. Presenters have to be very careful to present *Drosophila* as a useful model organism for understanding humans but not go too far and leave people with the idea that flies have human organs or human neurological disorders, much less human feelings, human thoughts, etc. To be fair, researchers themselves often fall into this trap themselves and heavily anthropomorphize their work to obtain funding and generate publications, so it is not a problem exclusive to the lay public (for a review, see Ref. 21). In this regard, these exercises also serve as a powerful way to force researchers to think carefully about the language they use when talking to the public about their own research.

Conclusions

From an early stage of a scientist’s career, communicating with other scientists takes priority over communicating with laypeople. As a result, professors, postdocs and students are primarily focused on communicating with other biologists and simply do not take the time to engage with the public in a systematic manner. Furthermore, as biological research becomes ever more detailed and specialized, it becomes harder and harder for active researchers to step back and explain their research to nonscientists. These factors are combining to create a disconnect between scientific communities and the taxpayers who ultimately fund research (12a, 20).

As invertebrate biologists working with *Drosophila*, we are focused on using our model organism as a tool to 1) uncover conserved principles in biology and 2) gain insight into how the human body functions. In our field, we encounter many researchers who are making important contributions to the scientific record but who are unenthusiastic about engaging with the public. On the other hand, we also come across many laypeople who have little or no understanding of the value of basic research on *Drosophila* and other invertebrates. Our goal here was to create a set of simple teaching modules that can help bridge this gap.

In the present study, we created a set of *Drosophila*-based teaching modules that explain to laypeople why basic research on an invertebrate animal is worthwhile. The exercises convey principles of biology and are effective over a wide range of ages. Overall, this work shows how *Drosophila* can be used to promote basic biomedical research among nonscientists.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

All authors contributed equally to this work.

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